REMARKS

Status Summary

Claims 1-36 are now pending in the subject U.S. patent application. Claims 17-20 and 22-36 have been withdrawn pursuant to a Restriction/Election Requirement issued by the U.S. Patent and Trademark Office (hereinafter "the Patent Office"). Accordingly, claims 1-16 and 21 have been examined by the Patent Office. Claims 1-16 and 21 presently stand rejected.

The Patent Office has objected to the disclosure upon the assertion that the specification contains an embedded hyperlink and/or other browser-executable code.

Claims 1-16 and 21 have been rejected under 35 U.S.C. §102(a/e) upon the contention that the claims are anticipated by PCT Patent Application Publication WO 02/26192 to Van Meir et al. (hereinafter "Van Meir et al.").

Claims 9-14 have been canceled herein. Claim 1 has been amended to more particularly recite the presently disclosed subject matter. Support for the amendments can be found throughout the specification, including particularly at page 6, line 31, through page 7, line 3; page 8, lines 5-9; and Figure 4. No new matter has been added.

Reconsideration of the application based on the amendments and arguments set forth herein is respectfully requested.

Of note, applicants respectfully submit that the filing date as listed on the face of the Official Action is believed to be incorrect. The correct filing date is believed to be March 24, 2005.

Response to the Objection to the Specificaiton

The Patent Office has objected to the disclosure upon the assertion that the specification contains an embedded hyperlink and/or other browser-executable code. The Patent Office asserts that the embedded hyperlinks located at page 28, line 5 and page 31, line 22 must be deleted.

In response, applicants respectfully submit that the specification has been amended hereinabove. In particular, the embedded hyperlinks located at page 28, line 5 and page 31, line 22, have been deleted. As such, applicants respectfully submit that the instant objection has been addressed. No new matter has been added.

Response to the Rejection of Claims under 35 U.S.C. § 102(a/e)

Claims 1-16 and 21 have been rejected under 35 U.S.C. §102(a/e) upon the contention that the claims are anticipated by Van Meir et al. The Patent Office contends that Van Meir et al. teaches each and every element of claims 1-16 and 21.

The contentions of the Patent Office as summarized above with respect to the rejected claims are respectfully traversed as described below.

Preliminarily, applicants note that it is well settled that for a cited reference to qualify as prior art under 35 U.S.C. §102, each element of the claimed subject matter must be disclosed within the reference. "It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention." Hybritec, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986). Thus,

applicants respectfully submit that for the cited reference to be an anticipation reference under 35 U.S.C. §102, the reference must disclose each and every element of the claimed subject matter.

Initially, applicants respectfully submit that dependent claims 9 to 14 have been canceled herein. As such, the instant rejection as applied to these claims is rendered moot.

Without acquiescing to the contentions of the Patent Office, applicants respectfully submit that independent claim 1 has been amended herein as follows:

> 1. An adenovirus vector comprising an adenovirus gene and a transgene, each under the transcriptional control of a transcriptional regulatory element (TRE) comprising a minimal promoter and a hypoxia responsive element (HRE), wherein the transgene is a suicide gene selected from the group consisting of a TNF-α gene, a Trail gene, a Bax gene, an HSV-tk gene, a cytosine deaminase gene, a p450 gene, and a diphtheria toxin gene, an s-Flt1 gene, and an ex-Flk1 gene.

Support for the amendments to claim 1 can be found throughout the specification as filed and particularly at page 6, line 31, through page 7, line 3; page 8, lines 5-9; and Figure 4. No new matter has been added.

Accordingly, claim 1 is directed to an adenovirus vector comprising an adenovirus gene and a transgene, wherein the transgene is a suicide gene. Applicants respectfully submit that Van Meir et al. does not teach an adenovirus vector comprising an adenovirus gene and a transgene, wherein the transgene is a suicide gene selected from the group consisting of a TNF-α gene, a Trail gene, a Bax gene, an HSV-tk gene, a cytosine deaminase gene, a p450 gene, and a diphtheria toxin gene, an s-Flt1 gene, and an ex-Flk1 gene, as currently recited in claim 1.

The Patent Office refers to page 19, line 28, through page 20, line 1 of Van Meir et al., which recites "Recombinant viruses of the invention can be further engineered to contain a gene that allows for the termination of viral propagation with an exongenous agent, such as thymidine kinase, which would render them susceptible to ganciclovir". *See*, page 7 of the Official Action. Accordingly, it appears that the Patent Office is asserting that this disclosure in Van Meir et al. anticipates the subject matter of claim 14, now incorporated into amended claim 1.

However, applicants respectfully disagree. In particular, the above-noted reference to Van Meir et al. is believed to be directed to the termination of viral propagation, whereas a suicide gene as recited in amended claim 1 is a gene that causes a cell to die. Applicants direct the Patent Office's attention to page 35, line 18; through page 36, line 11, of the specification as filed which recites:

> As used herein, the term "suicide gene" refers to a gene that encodes a polypeptide that causes a cell that produces that polypeptide to die. A suicide gene can encode a gene that causes cell death directly, for example by inducing apoptosis. Such a gene is referred to as an "apoptosis-inducing gene", and includes, but is not limited to TNF-α (Idriss & Naismith, 2000), Trail (Srivastava, 2001), Bax, and Bcl-2 (Shen & White, 2001). Other genes that encode proteins that kill cells directly include bacterial toxin genes, which are normally found in the genome of certain bacteria and encode polypeptides (*i.e.* bacterial toxins) that are toxic to eukaryotic cells. Bacterial toxins include but are not limited to diphtheria toxin (Frankel *et al.*, 2001).
>
> Alternatively, a suicide gene can encode a polypeptide that converts a prodrug to a toxic compound. Such suicide prodrug converting enzymes include, but are not limited to the HSV-tk polypeptide, which converts ganciclovir to a toxic nucleotide analog (Freeman *et al.*, 1996); cytosine deaminase, which converts the non-toxic nucleotide analog 5-fluorocytosine into a toxic analog, 5-fluorouracil (Yazawa *et al.*, 2002); and cytochrome p450, which converts certain aliphatic amine N-oxides into toxic metabolites (Patterson, 2002).

> Additionally, a suicide gene can encode a polypeptide that interferes with a signal transduction cascade involved with cellular survival or proliferation. Such cascades include, but are not limited to, the cascades mediated by the Flt1 and Flk1 receptor tyrosine kinases (reviewed in Klohs, *et al.*, 1997). Polypeptides that can interfere with Flt1 and/or Flk1 signal transduction include, but are not limited to, a soluble Flt1 receptor (s-Flt1; Shibuya, 2001) and an extracellular domain of the Flk-1 receptor (ex-Flk1; Lin *et al.*, 1998).

(emphasis added). Accordingly, applicants respectfully submit that a gene that allows for the termination of viral propagation with an exongenous agent is not tantamount to a suicide gene, as recited in claim 1. Therefore, applicants respectfully submit that it would be improper to rely on the above-noted reference in Van Meir et al. to support an anticipatory rejection of amended claim 1.

Accordingly, applicants respectfully submit that Van Meir et al. does not teach each and every element of independent claim 1. Thus, applicants respectfully submit that the instant 35 U.S.C. §102(a/e) rejection of independent claim 1 has been addressed. Accordingly, applicants respectfully request that the instant rejection be withdrawn at this time. A Notice of Allowance directed to claim 1 is also respectfully requested.

Applicants further submit that claims 2-8, 15-16 and 21 depend from independent claim 1. Accordingly, the instant 35 U.S.C. §102(a/e) rejection of these claims has also been addressed. Thus, applicants respectfully request that the instant rejection be withdrawn at this time. A Notice of Allowance directed to these claims is also respectfully requested.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

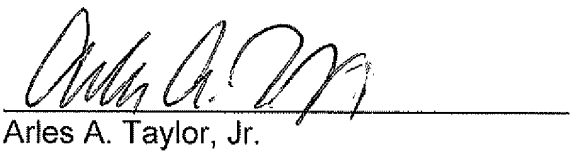
If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any additional fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: February 19, 2008 By: 

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